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DENNISON, SCHULTZ, DOUGHERTY & MACDONALD
1727 KING STREET
SUITE 105
ALEXANDRIA, VA 22314

| EXAMINER | |
|---|---|
| QAZI, SABIHA NAIM | |

| ART UNIT | PAPER NUMBER |
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| 1616 | |

DATE MAILED: 04/19/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/423,109 | PARIS ET AL. | |
| | Examiner | Art Unit | |
| | Sabiha Qazi | 1616 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *01 February 0206*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *3,4,7,8,13,18-21,25,26,30 and 31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *3, 4, 7, 8, 13, 18-21, 25, 26, 30, and 31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

**Non-Final Office Action**

Claims 3, 4, 7, 8, 13, 18-21, 25, 26, 30, and 31 are pending, all of which are rejected.

Acknowledgment is made of the Response filed on February 2, 2006.

**Response to Remarks**

- The Applicants' arguments regarding the new matter rejection and the written description rejection were found persuasive. Therefore, these rejections are withdrawn.
- The Applicants' arguments regarding the rejection over PLUNKETT et al and BLANC et al are not found persuasive. The Applicants argue that the ranges claimed in the instant invention are not taught in the prior art. The Applicants have not shown any comparison and/or criticality. What are the unexpected results? What benefits are there to these ranges? There is no comparison with the prior art seen in the Declaration.

  Normally, change in temperature, concentration, or both, is not a patentable modification; however, such changes may impart patentability to a process if the ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from results of prior art; such ranges are termed "critical" ranges, and applicant has burden of proving such criticality; even though applicant's modification results in great improvement and utility over prior art, it may still not be patentable if the modification was within the capabilities of one skilled in the art; more particularly, where the general conditions of the claim are

disclosed in the prior art, it is not inventive to discover optimum or workable ranges by routine experimentation. In re Aller et al. 105 USPQ 233.

**It is well established that merely selecting proportions and ranges is not patentable absent a showing of criticality.** In re Becket, 33 U.S.P.Q. 33 (C.C.P.A. 1937). In re Russell, 439 F.2d 1228, 169 U.S.P.Q. 426 (C.C.P.A. 1971).

It is a general rule that merely discovering and claiming a new benefit of an *old* process cannot render the process again patentable. Nor can patentability be found in differences in ranges recited in the claims. When the difference between the claimed invention and the prior art is some range or other variable within the claims, the applicant must show that the particular range is *critical*, generally by showing that the claimed range achieves unexpected results relative to the prior art range. In re Woodruff, 16 USPQ2d 1934.

**Summary**

The previous 112 rejections are withdrawn. The previous 103 rejection stands. A new 112 scope of enablement rejection has been added.

***Information Disclosure Statement***

The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be

incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

## Copending Applications

Applicants must bring to the attention of the examiner, or other Office official involved with the examination of a particular application, information within their knowledge as to other copending United States applications, which are "material to patentability" of the application in question. MPEP 2001.06(b). See Dayco Products Inc. v. Total Containment Inc., 66 USPQ2d 1801 (CA FC 2003).

### *Double Patenting*

1. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

2. Claims 3, 4, 7, 8, 13, 18-21, 25, 26, 30, and 31 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,831,073. Although the conflicting claims are not identical, they are not patentably distinct from each other because presently claimed invention is considered obvious over claims 1-6 of US '073.

3. Instant claims differ from the reference in claiming "correcting estrogen deficiency" and "preventing osteoporosis" wherein the calims of issued patent cites ""a method of treating estrogenic deficiencies" and "avoiding the appearance of osteoporosis" which are obvious.

4. It would have been obvious to one skilled in the art to prepare addition beneficial composition useful for avoiding osteoporosis and to treat estrogenic deficiencies. Motivation has been provided in the claims and also in the specification. One who is faminliar with the art would have been motivated to prepare compositions of estradiol ester such as the combination of estradiol valerate and nomegesterol acetate (NOMAC) and use for the treatment of estrogen deficiencies and to avoid osteoporosis.

**Claim Rejections - 35 USC § 112**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

*The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.*

Claim 3, 4, 7, 8, 13, 18-21, 25, 26, 30, and 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the combination of NOMAC and estradiol valerate, does not reasonably provide enablement for preventing osteoporosis and correcting estrogen deficiencies. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

There is no support to show how osteoporosis can be prevented or estrogen deficiencies can be corrected in the disclosure.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in *In re Wands*, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The claims are drawn to a method of correction estrogen deficiencies and preventing osteoporosis in menopausal women.

(2) The predictability or unpredictability of the art

The "predictability or lack thereof" in the art refers to the ability of one skilled in the art to extrapolate the disclosed or known results to the claimed invention. If one skilled in the art can readily anticipate the effect of a change within the subject matter to which the claimed invention pertains, then there is predictability in the art. On the other hand, if one skilled in the art cannot readily anticipate the effect of a change within the subject matter to which that claimed invention pertains, then there is lack of predictability in the art. Accordingly, what is known in the art provides evidence as to the question of predictability. In particular, the court in *In re Marzocchi*, 439 F.2d 220, 223-24, 169 USPQ 367, 369-70 (CCPA 1971), stated:

[I]n the field of chemistry generally, there may be times when the well-known unpredictability of chemical reactions will alone be enough to create a reasonable doubt as to the accuracy of a particular broad statement put forward as enabling support for a claim. This will especially be the case where the statement is, on its face, contrary to generally accepted scientific principles. Most often, additional factors, such as the teachings in pertinent references, will be available to substantiate any doubts that the asserted scope of objective enablement is in fact commensurate with the scope of protection sought and to support any demands based thereon for proof.

The scope of the required enablement varies inversely with the degree of predictability involved, but even in unpredictable arts, a disclosure of every operable species is not required. A single embodiment may provide broad enablement in cases involving predictable factors, such as mechanical or electrical elements. *In re Vickers*, 141 F.2d 522, 526-27, 61 USPQ 122, 127 (CCPA 1944); *In re Cook*, 439 F.2d 730, 734, 169 USPQ 298, 301 (CCPA 1971). However, in applications directed to inventions in arts where the results are unpredictable, the disclosure of a

single species usually does not provide an adequate basis to support generic claims. *In re Soll*, 97 F.2d 623, 624, 38 USPQ 189, 191 (CCPA 1938). In cases involving unpredictable factors, such as most chemical reactions and physiological activity, more may be required. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993); *In re Vaeck*, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). This is because it is not obvious from the disclosure of one species, what other species will work. See MPEP 2164.03.

(3) The breadth of the claims

The claims are broad because the Applicants are claiming "correcting estrogen deficiencies". There are many different types of estrogen deficiencies; they have only ***one*** example (endometrium) to support their claim for ***all*** estrogen deficiencies, as shown in the Disclosure. See Plunkett et al. (US Re. 36,247) and Blanc et al. (Clinical Therapeutics, 1998), 20(5), 901-912).

In re Fisher, 427 F.2d 833, 166 USPQ 18 (CCPA 1970) (contrasting mechanical and electrical elements with chemical reactions and physiological activity). See also In re Wright, 999 F.2d 1557, 27 USPQ2d 1510 (Fed. Cir. 1993); In re Vaeck, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). It is not obvious from the disclosure of one species, what other species will work.

In re Dreshfield, 110 F.2d 235, 45 USPQ 36 (CCPA 1940), gives this general rule: "It is well settled that in cases involving chemicals and chemical compounds, which differ radically in

their properties it must appear in an applicant's specification either by the enumeration of a sufficient number of the members of a group or by other appropriate language, that the chemicals or chemical combinations included in the claims are capable of accomplishing the desired result."

(4) The amount of direction or guidance presented

There is no guidance needed to enable one skilled in the art to successfully prevent osteoporosis and/or correct any estrogen deficiencies in the disclosure. The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling. >See, e.g., *Chiron Corp. v. Genentech Inc.*, 363 F.3d 1247, 1254, 70 USPQ2d 1321, 1326 (Fed. Cir. 2004) ("Nascent technology, however, must be enabled with a 'specific and useful teaching.' The law requires an enabling disclosure for nascent technology because a person of ordinary skill in the art has little or no knowledge independent from the patentee's instruction. Thus, the public's end of the bargain struck by the patent system is a full enabling disclosure of the claimed technology."

(5) The presence or absence of working examples

The disclosure does not contain enough examples to give guidance needed to enable one skilled in the art to prevent osteoporosis and/or correct any estrogen deficiencies. A disclosure should contain representative examples, which provide reasonable assurance to one skilled in the art that the compounds fall within the scope of a claim will possess the alleged activity. See In re Riat et al. (CCPA 1964) 327 F2d 685, 140 USPQ 471; In re Barr et al. (CCPA 1971) 444 F 2d 349, 151 USPQ 724.

(6) The quantity of experimentation necessary

Since there is no guidance and/or direction provided by the Applicants, one skilled in the art would have to go through undue experimentation to make and/or use the instant invention.

The first paragraph of 35 USC 112 requires "*...such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains...*" The instant invention fails to meet this requirement, as it lacks such full, clear, and concise manner as to enable any person skilled in the art to which it pertains to make and/or use the invention.

**Claim Rejections - 35 USC § 103**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be *obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject*

*matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patent ability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patent ability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 3, 4, 7, 8, 13, 18-21, 25, 26, 30 and 31 are rejected under 35 U.S.C. 103(a) as obvious over Plunkett et al. (US Re. 36,247) and Blanc et al. (Clinical Therapeutics, 1998), 20(5), 901-912). Both the references teach the art, which embraces instantly, claimed invention. See the entire documents, especially cited below.

**1. Determining the scope and contents of the prior art.**

Plunkett teaches a method of hormonal treatment for menopausal disorders involving continuous administration of progestagens and estrogens. See the entire document especially lines 40-51, col. 2; lines 63-67, col. 2; lines 1-67, col. 3; lines 18-25, and lines 1-5, col. 4; lines 46-50, col. 6.

The reference teaches continuous and uninterrupted administration of progestagen and estrogen. The actual unit dosage are selected according to conventionally known methods, e.g. body weight of patient and biological activity of hormones with the ultimate goal of producing the desired result with minimum quantities of hormones. It does not disclose specifically nomegesterol acetate.

Blanc et al teaches continuous hormone replacement therapy combining nomegesterol acetate and gel, patch or oral estrogen. See the abstract of the invention; cols 1 and 2 on page 903col. 2 on page 904, Table 1 on page 905Figure on page 906 ; Table II on page 907. Prior art also teach that bleeding occurs when treatment is discontinued.

**2. Ascertaining the differences between the prior art and the claims at issue.**

Instant claims are drawn to a method of treating deficiencies of estrogen by continuously administering a combination of estrogen and nomagesterol acetate. Blanc et al. teach the same combination, the ranges of the amounts overlap with the prior art teaching. Prior art teaches estradiol, 2 mg/dose whereas presently claimed amount is 0.3-3 mg and nomegesterol 2.5 mg/d whereas presently claimed amount 0.3 to 1.25 mg. The Plunkett et al differs from the instant invention in that it does not specifically name nomegesterol acetate. Presently claimed invention does not clearly state what is the amount of the steroids per dose per day.

**3. Resolving the level of ordinary skill in the pertinent art.**

It would be obvious to one skilled in the art at the time of invention to prepare a composition of NOMAc and estrogen to administer continuously combination of estrogen and nomegesterol as cited above.

**4. Considering objective evidence present in the application indicating obviousness or nonobviousness.**

Motivation is to use estrogen and progestagen continuously as taught by Plunkett et al. and use nomegesterol as progestagen because it gives in all patients regular, progestagen-induced withdrawal bleed each month; and histological, ultra structural and biochemical changes were induced within the endometrium by all doses (0.5 mg, 1.0 mg; and 2.5 mg) is a potent progestogen. Blanc et al. teach same combination as combination of nomegestrol and estradiol. Thus, there has been ample motivation provided by the teachings of both the references cited above to prepare the instant invention in absence of any criticality or unexpected results.

Claim 31 is drawn to composition useful for hormone replacement therapy. The Examiner would like to emphasize that the two different intended uses are not distinguishable in terms of the composition, see *In re Thuau,* 57 USPQ 324; *Ex parte Douros,* 163 USPQ 667; and *In re Craige,* 89 USPQ 393. Composition is therefore considered obvious.

It has been established by the courts that a single species is seldom, if ever, sufficient to support a generic claim. In re Shokal, 242 F.2d 771, ___, 113 U.S.P.Q. 283, 285 (C.C.P.A.

1957). See also, In re Grimme, 274 F.2d 949, ___, 124 U.S.P.Q. 499, 501 (C.C.P.A. 1960) (the naming of a member of a genus or subgenus is not a proper basis for claiming the whole group).

Objective evidence of nonobviousness must be commensurate in scope with the scope of the claims. In re Tiffin, 171 USPQ 294. A showing limited to a single species can hardly be considered probative of the invention's nonobviousness in view of the breadth of the claims.

The new Declaration was considered, but was not found persuasive. The claims are too broad. Example 1 is drawn to the study on symptoms related to estrogen deficiencies by using .625 mg of NOMAC and .5mg of E2, 1.25 mg of NOMAC and 1mg of E2, and a placebo. Example 2 is drawn to the study of preventing osteoporosis. The results show that E2/NOMAC combinations of the invention were able to decrease bone resorption, which the Applicants directly link to preventing osteoporosis. The Examiner respectfully disagrees; the decrease of bone resorption has not been shown and/or explained to prevent osteoporosis by all the combinations as claimed.

There is motivation provided by the prior art to select NOMAC because at high doses there is no bleeding pattern and have different effect on endometrium. Examiner notes, paragraph after Table 3 on page 4 of the declaration that applicant has cited the advantages which are known in the art.

In the light of the forgoing discussion, the Examiner's ultimate legal conclusion is that the subject matter defined by the instant claims would have been obvious within the meaning of 35 U.S.C. 103(a).

**Communication**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sabiha Qazi whose telephone number is 571-272-0622. The examiner can normally be reached on any business day.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Sreeni Padmanabhan can be reached on 571-272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

S. Qazi

SABIHA QAZI, PH.D
PRIMARY EXAMINER

**Friday,**
**April 14 2006**